

**Notice of Allowability**

Application No.

10/623,036

Examiner

Samuel Woolwine

Applicant(s)

STEMMER, WILLEM P.C.

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to papers filed 4/18/2007, 4/24/2007 and 5/7/2007.
2. ☒ The allowed claim(s) is/are 1-5 and 33-39.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All    b) ☐ Some\*    c) ☐ None    of the:
    1. ☐ Certified copies of the priority documents have been received.
    2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

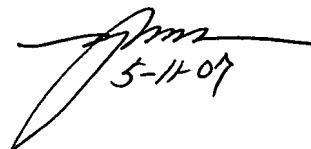
\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.  
**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
  5. ☐ CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
    - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
      - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
    - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08),  
Paper No./Mail Date 4/24/2007
4. ☐ Examiner's Comment Regarding Requirement for Deposit  
of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413),  
Paper No./Mail Date \_\_\_\_\_
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other \_\_\_\_\_

  
5-11-07

### **EXAMINER'S AMENDMENT**

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Sharon Fujita on 5/1/2007 and has been applied to the claims filed 5/7/2007, which differ from the claims filed 4/18/2007 only by the addition of claim 39.

The application has been amended as follows:

Change claim 1 to the following:

A method for selecting from or screening a library of recombinant proteins to identify a recombinant protein having a desired functional property, said method comprising:

- a) randomly fragmenting a template double-stranded DNA into a plurality of double-stranded fragments of a desired size;
- b) adding to said plurality of double-stranded fragments one or more single- or double-stranded oligonucleotides, wherein said single- or double-stranded oligonucleotides comprise areas of identity and areas of heterology to the template double-stranded DNA;
- c) denaturing said plurality of double-stranded fragments and said oligonucleotides to form a population of single-stranded fragments;

d) incubating said population of single-stranded fragments from step c) with a polymerase under conditions which result in the annealing of said single-stranded fragments at said areas of identity to form pairs of annealed fragments, said areas of identity being sufficient for one member of a pair to prime replication of the other member of the pair, thereby forming mutagenized double-stranded DNA molecules;

e) repeating steps c) and d) for a desired number of cycles, wherein repeated step c) further comprises denaturing the mutagenized double-stranded DNA molecules formed in step d) in previous cycles, thereby forming a library of mutagenized double-stranded DNA molecules;

f) expressing a library of recombinant proteins encoded by said library of mutagenized double-stranded DNA molecules from step e); and

g) selecting or screening said library of recombinant proteins to identify a recombinant protein with a desired functional property.

Change claim 2 to the following:

The method of claim 1 wherein the concentration of a specific double-stranded fragment in the plurality of double-stranded fragments in step b) is less than 1% by weight of the total amount of DNA in the combined plurality of double-stranded fragments and single- or double-stranded oligonucleotides in step b).

Change claim 3 to the following:

The method of claim 1 wherein the number of different specific double-stranded fragments in step a) comprises at least about 100.

Change claim 4 to the following:

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The method of claim 1 wherein the size of the double-stranded fragments in step a) is from about 5 bp to 5 kb.

Change claim 5 to the following:

The method of claim 1 wherein the size of the mutagenized double-stranded DNA molecules in the library of mutagenized double-stranded DNA molecules in step e) is from about 50 bp to 100 kb.

Change claim 33 to the following:

The method of claim 1 wherein the template double-stranded DNA encodes a wild-type protein.

Change claim 37 to the following:

The method of claim 1 wherein the size of the double-stranded fragments in step a) is from about 10 bp to 1000 bp.

Change claim 38 to the following:

The method of claim 1 wherein the size of the double-stranded fragments in step a) is from about 20 bp to 500 bp.

The following is an examiner's statement of reasons for allowance:

The claimed methods describe a novel method for generating a library of mutagenized DNA molecules, expressing said DNA molecules in the form of a recombinant proteins and screening/selecting the collection of recombinant proteins for proteins having a desired functional property. The novelty lies in the method by which the library of mutagenized DNA molecules is generated, which involves the random

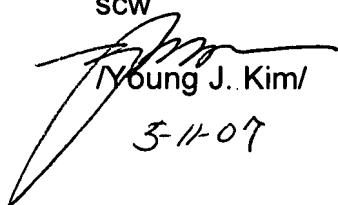
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fragmentation of a starting template DNA, the addition of single- or double-stranded oligonucleotides having both regions of identical to the template and regions that are not identical to the template, and the repeated denaturing, reannealing, and treatment of the DNA molecules with a polymerase. Such a method is not taught or suggested in the prior art.

Furthermore, based on the filing of terminal disclaimers, the double patenting rejections made in the Office action dated 11/30/2005 are withdrawn.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

SCW

  
/Young J. Kim/  
3-11-07